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09/181,108	10/28/98	MILLER	B 176/60440-(1

EXAMINER	
CELSA, B	
ART UNIT	PAPER NUMBER
1627	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.	Applicant(s)
09/181,108	Miller et al.
Examiner	**Group Art Unit**
Bennett Celsa	1627

☒ Responsive to communication(s) filed on *Dec 20, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-10 and 41* is/are pending in the application.

Of the above, claim(s) *8 and 9* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 10, and 41* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

Applicant's amendment (with Rule 132 Declarations) dated 12/20/00 in paper numbers 16 and 17 are hereby acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-10 and 41 are currently pending.

Claims 1-7, 10 and 41 are under consideration.

Claims 8-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Election/Restriction

2. Applicant's election without traverse of the species of bis-N-[2-(2-aminomethyl)-1-methyl pyrrolidine]salicyladimanate Zinc II in Paper No. 13 which reads on claims 1-7 and 10 in response to the Supplemental Election of Species in paper no. 11 was acknowledged.

3. Claims 8-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objection (s) and/or Rejection (s)

The submitted Rule 132 Katz declarations by the present inventors has overcome the rejection of claims 1-7 and 10 under 35 U.S.C. 102(a) as being anticipated, or in the alternative as obvious over Klekota et al. Tetrahedron Letters Vol. 38, No. 50 (12/15/97).

Applicant's amendment incorporating metal/metal ions as the ligand has overcome the rejection of claims 1-6 and 10 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Benner, U.S. Pat. No. 5,958,702 (9/99: filed 2/95).

Applicant's amendment has overcome the rejection of claims 1-7 and 10 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment has overcome the rejection of 1-7 and 10 under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabled.

Applicant's amendment has overcome the rejection of claims 1-7 and 10 under 35 U.S.C. 112, second paragraph, as being indefinite.

New Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

4. Claims 1-7, 10 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There appears to be no specification support for the term "target molecule" nor has applicant's representative pointed to where such support exists. Perhaps amending to recite "biological receptor" may be considered in lieu of this term (e.g. see specification page 16).

5. Claims 1-7, 10 and 41 are rejected under 35 U.S.C. 103(a) as obvious over Barton US Pat. No. 4,980,473 (12/90) and Benner, U.S. Pat. No. 5,958,702 (9/99: filed 2/95).

Barton discloses (chiral) coordination complexes of transition metals which comprise "at least two non-biopolymer ligands" (e.g. three ligands which comprise unsubstutituted/substituted 1,10 phenanthrolines, racemers and isomers) which contain a "recognition element" which "targets" DNA (e.g. see abstract, examples and patent claims). For example Barton discloses a cobalt complex with ligands which comprise 1,10 phenanthroline and a list of 12 "substituted" phenanthrolines" (e.g. hydroxy, phenyl, substituted phenyl intercalotors etc.) which include their racemers (e.g. see col. 7, lines 1- 40) which would encompass at least 169 distinct complexes (e.g. 13x13 representing 13 unsubstitued and substituted and their D/L enantiomers). These

complexes are then screened for their binding to DNA (e.g. by intercalation: see. bottom of col. 7 to top of col. 8).

The Barton reference composition differs from the presently claimed invention insofar that the presently claimed invention "collects together" (e.g. combinatorializes) complexes such as those in Bartow for screening.

However, the Benner reference discloses the advantages of utilizing soluble "combinatorial library" techniques for generated diverse structures which could then be advantageously screened e.g. using a "receptor-assisted combinatorial chemistry" (e.g. see col. 2-5).. In this regard, the Benner reference discloses the versatility of this approach as utilized over a wide range of complexed atoms, groups of atoms or ions. In this regard, the Benner reference discloses the use of biopolymer or non-biopolymer ligands

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to apply the Benner combinatorial protocol to the Barton generic of transition metal phenanthroline complexes which contain "recognition elements" that are "capable of" binding a "target molecule" (e.g. DNA) in view of the advantages of utilizing combinatorial techniques (e..g increasing diversity) as well as the advantages of utilizing improved screening techniques (e.g. receptor-assisted combinatorial chemistry) as disclosed in the Benner reference teaching.

Additionally, scaling the library up by increasing the number of library members (e.g. increase the number of Barton substituted phenanthroline ligand) to attain increased diversity is

suggested by the Benner reference and would in any event represent mere optimization to one of ordinary skill in the art.

Outstanding Objection (s) and/or Rejection (s)

6. Claims 1-7 and 41 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Blackborow et al., J. Chem. Res (S) Jan. 1978 page 119..

Blackborow et al. disclose a combinatorial library of a "plurality of at least six different complexes" which comprises a complex having a complexing agent (e.g a transition metal: zinc) and monomers (which would include D/L optical configurations and thus are distinctly different ligands), dimers (of two distinctly different structure) and/or trimers in which the ligands are salicyclaldiminatozine derivatives which clearly anticipate claims 1-5 and 7. The Blackborrow et al. reference complexes further comprise "substituted (e.g. methyl, isopropyl etc.) or unsubstituted phenyl groups" which constitute "recognition elements" within applicant's definition since they are "capable of" "binding" a "target molecule". In this regard, the reference complex contains chemical structure explicitly within the claimed scope of defined "recognition element" (e.g. see amended claim 6) and thus "inherently" must "bind" or be "capable of binding" (e.g. can be derivatized to bind) a particular "target molecule" .

Alternatively, the reference complex may be interpreted to possess "recognition elements" that are "capable of" being classed as "DNA intercalators" or "major or minor groove DNA binders" within the open ended specification definition of these terms (e.g. see specification pages

7-10 which encompass "hydroxy"; "alkoxy" or "amine" groups which are within the scope of the presently claimed invention) with these ligands being either phenyl substituted derivative which further cormprise an amine moeity. Additionally, it is further noted that the Blackborrow reference further contains the "Nme" substituents which is an "amine" group (e.g. an alkylamine group).

Accordingly, the Blackborrow et al. reference library complexes contains chemical structure which meets both the specific claimed structure (e..g metal atom/ion) as well as the presently claimed functional structure (e.g. "non-biopolymer ligands" , "recognition elements").

The Examiner lacks the facilities to determine whether the reference ligands are capable of functioning under the overly broad specificaition definition for "recognition elements".

Discussion

Applicant's arguments directed to the above 102/103 rejection over the Blackborow et al. Reference were considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that the above anticipation rejection was rewritten in order to address the claims, as amended.

Applicant argues that that salicylamidimines of Blackborrow fail to contain a "recognition element capable of binding a target molecule".

The Examiner respectfully disagrees. As discussed above the Blackborrow complexes contain chemical structure which is within the scope of the chemical structure described as constitituting a "recognition element" (e.g. substituted amine and/or a "substituted or

unsubstituted phenyl group") or alternatively contains chemical structure which can be made "capable of" binding a "target molecule" .

Applicant further argues that the reference fails to provide motivation to modify the salicyclaldimines to generate a useful library.

As discussed above, the chemical structure of the reference library members already meet the structural requirements of the presently claimed libraries; redering modification unnecessary. In this regerd, the reference library compound structure contains chemical structure (e.g. substituted/unsubstituted phenyl, substituted amine) which are "recognition elements" per se or althernatively represents chemical structure which is "capable of" binding a target molecule.

Thus, the above rejection, as modified, is hereby maintained.

7. Claims 1-7, 10 and 41 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jacobsen et al. WO 98/12156 (3/98)..

Jacobsen et al. disclose a combinatorial approach for generating novel coordination complex mixtures of "at least 6" (e.g. see page 6, lines 5-10) by coordinating to a transition metal (e.g. including zinc: see e.g.. Page 6, lines 17-26) and ligands (e.g. non-biopolymer: see e.g. pages 25-31) to form bidentate, tridentate, tetradentate or even higher order metal chelating ligands (e.g. see page 6, lines 7-10; and abstract). Additionally, a large number of the reference ligands (e.g. see pages 25-31) comprise substituted and unsubstituted aryl and heterocyclic moietes which would constitute "recognition elements" that are capable of being classed as "DNA intercalators"

or "major or minor groove DNA binders" within the open ended specification definition of these terms (e.g. see specification pages 7-10 which encompass aryl and heterocycles as well as "hydroxy"; "alkoxy" or "amine" groups which are within the scope of the presently claimed invention) with these ligands being either phenyl or substituted derivative which further comprise an amine moeity. Alternatively , the selection of such an intercalating ligand would be obvious to one of ordinary skill in the art. Reference claims 29-30 and Fig. 1-11 disclose specific reference library combinations which anticipate the presently claimed invention.

Additionally, the reference also teaches that the reaction of the metal(s) with the library of PBM to form a combinatorial library of potential catalysts comprising metal complexes can occur in "solution", on a soluble support or utilizing insoluble polymeric supports (e.g. see page 39) which would serve to anticipate newly added claim 41 addressing the presence of the library in either "aqueous solution" or I "suspension.

It is noted that the Examiner lacks the facilities to determine whether the reference ligands are capable of functioning under the overly broad specificaition definition for "recognition elements".

Discussion

Applicant's arguments directed to the above 102/103 rejection over the Jacobsen et al. reference were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant first argues that Jacobsen fails to teach a combinatorial library where complexes in the library are formed of a metal atom joined by a labile coordinate bond to non-biopolymer ligands containing a recognition element.

Applicant is misguided since the Jacobsen reference clearly teaches the use of a library comprising "nonbiopolymer" ligands and a turn element which serve as a potential binding moiety (PBM) which comprise groups which are clearly within the scope of a "recognition element" as broadly described and presently claimed. The Jacobsen reference further explicitly teaches the formation of a library of transition metal catalysts comprising a metal coordination complex which result upon the addition of metal(s) to the PBM's whether in solution or while attached to a solid support (e.g. see Abstract, figures and claims). As pointed out in the rejection (e.g. reference page 6) the reference discloses the use of 100-10,000 *different* PBM's with the selection of "The chelating agent and metal ... so that the chelating agent *can coordinate the metal ion* with a degree of stability great enough that the metal ion will remain sequestered by the chelating agent" (emphasis provided). Accordingly, the reference would be expected to generate libraries of metal coordination complexes (which may serve as catalysts) which are within the scope of the presenlty claiimed invention with respect to both numbers and chemical composition. It is again noted that the Examiner lacks the facilities to perform experimental testing.

Applicant argues that the Jacobsen reference teaches away since it requires replacing the "turn element" with a metal to arrive at the presently claimed libraries..

Applicant is failing to interpret the reference teaching taken as a whole which specifically describes the addition of metal(s) to the library of reference ligands (which may include the turn element) which results in the formation of transition metal complex libraries within the scope of the presently claimed invention. Accordingly, there is no need to substitute the turn element with a metal as argued by applicant.

Thus, the above 102/103 rejection is hereby maintained.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

March 22, 2001

BENNETT CELSA
PRIMARY EXAMINER